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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
09/554,567	09/01/2000	Adriano Aguzzi	6458.US.01	2914
7590 12/10/2004 Steven F Weinstock			EXAMINER WINKLER, ULRIKE	
D 377 AP6D Abbott Park, IL 60064-6050			1648	
			DATE MAILED: 12/10/2004	

Please find below and/or attached an Office communication concerning this application or proceeding.

		Application No.	Applicant(s)	
Office Action Summary		09/554,567	AGUZZI ET AL.	
		Examiner	Art Unit	
		Ulrike Winkler	1648	
Period fo	The MAILING DATE of this communication apports. Peoply	pears on the cover sheet with the c	orrespondence address	
THE - Exte after - If the - If NC - Failu Any	ORTENED STATUTORY PERIOD FOR REPL MAILING DATE OF THIS COMMUNICATION. nsions of time may be available under the provisions of 37 CFR 1.1 SIX (6) MONTHS from the mailing date of this communication. e period for reply specified above is less than thirty (30) days, a repl period for reply is specified above, the maximum statutory period re to reply within the set or extended period for reply will, by statute reply received by the Office later than three months after the mailing ed patent term adjustment. See 37 CFR 1.704(b).	136(a). In no event, however, may a reply be timely within the statutory minimum of thirty (30) days will apply and will expire SIX (6) MONTHS from a Cause the application to become ABANDONE.	nely filed s will be considered timely. the mailing date of this communication.	
Status			-	
1)🖂	Responsive to communication(s) filed on Augu	ust 3, 2004.		
2a)⊠	This action is <b>FINAL</b> . 2b) This action is non-final.			
3)□	Since this application is in condition for allowal closed in accordance with the practice under <i>E</i>			
Dispositi	on of Claims	-	0.0.210.	
5)□ 6)⊠ 7)□	Claim(s) 35-37 is/are pending in the application 4a) Of the above claim(s) is/are withdraw Claim(s) is/are allowed. Claim(s) 35-37 is/are rejected. Claim(s) is/are objected to. Claim(s) are subject to restriction and/o	wn from consideration.		
Applicati	on Papers	•	·	
	The specification is objected to by the Examine			
10) 🗌	The drawing(s) filed on is/are: a)☐ acce			
	Applicant may not request that any objection to the		` '	
	Replacement drawing sheet(s) including the correct The oath or declaration is objected to by the Ex			
Priority u	nder 35 U.S.C. § 119		•	
a)[	Acknowledgment is made of a claim for foreign  All b) Some * c) None of:  1. Certified copies of the priority documents  2. Certified copies of the priority documents  3. Copies of the certified copies of the prior  application from the International Bureau  ee the attached detailed Office action for a list of	s have been received. s have been received in Applicationity rity documents have been received u (PCT Rule 17.2(a)).	on No d in this National Stage	
Attachment	( <b>s</b> )			
2)	e of References Cited (PTO-892) e of Draftsperson's Patent Drawing Review (PTO-948) nation Disclosure Statement(s) (PTO-1449 or PTO/SB/08) No(s)/Mail Date	4) Interview Summary ( Paper No(s)/Mail Dat 5) Notice of Informal Pa 6) Other:	e	

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#### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 3, 2004 has been entered.

The amendment filed August 3, 2004 in response to the Office Action of November 14, 2003 is acknowledged and has been entered. Claims 35-37 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

## Claim Rejections - 35 USC § 103

The rejection of claims 35-37 under 35 U.S.C. 103(a) as being unpatentable over O'Rourke et al. (US Pat No. 6,165,784),and/or Korth et al. (Nature 6 November 1997; 390:74-77), in view of Kuroda et al. (Infection and Immunity 1983; 41:154-61) and/or Manuelidis et al. (Science 1978; 200:1069-1071) is maintained for reasons of record.

Applicants' arguments have been fully considered but have failed to persuade the Office to remove the instant rejection. Applicants' arguments are that the cited references of Kuroda et al. or Manuelidis et al. referred to the disease causing agent as being a <u>virus</u> instead of the instantly claimed <u>prion protein</u> (TSE infecting agent). The protein only theory of disease has only recently gained acceptance in the scientific community. The biochemist, Stanley Prusiner,

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whose discovery provided key insights into dementia-related diseases, won the 1997 Nobel Medicine Prize, Sweden's Karolinska Institute. The institute said Prusiner's work helped the world to understand more about Alzheimer's and Mad Cow disease through his discovery of the prion, a disease-causing agent like bacteria or viruses. Even today there are is still a small group scientists that do not believe the protein only theory. Both of the cited references were published at a time when the prion protein theory of disease was not generally accepted. Even if the references erroneously referred to the disease-causing agent as a virus this does not detract from the important observation made in the references.

In response to Applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5

USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the animal experiments show that the disease causing agent is found in B and T cells of infected animals. The method of detecting the infecting agent in the experiments was to inject the fractionated sample into disease free animals. The experiments clearly show that the disease-causing agent is present in the T and B cells. The two other references disclose using a different method of detecting the disease-causing agent, with antibodies. This method of detection is direct, takes less time and does not require lengthy incubations.

Kuroda et al. fractionated B cells and T cells from diseased animals and inoculated the fractionated samples into non-diseased animals. The experiments indicate that the disease

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causing agent obtained from the spleens of mice infected with the causative agent of Creutzfeldt-Jakob disease (CJD), can be injected into susceptible mice and transmit disease (see entire document, especially Tables 2 and 4). Thus Kuroda et al. teach a method to test for the presence of TSE byobtaining a sample of spleen, collecting B cells and T cells from the sample, and testing the B cells and/or T cells for the presence of the TSE agent.

Manuelidis et al. in 1978 established that collecting B cells and T cells from infected animals, by isolating the buffy coat, and injecting the buffy coat into disease free animals the animals came down with the disease. This established directly that the disease-causing agent is found in the buffy coat of blood. The reference also indicated that the hematogenous spread is implicated in man (see last paragraph).

O'Rourke et al. tests for TSE in lymphoid tissue using an antibody that serves as a ligand in various immunoassays, including immunohistochemistry, western immunoblots, and dot blots (see entire document, e.g., "Summary of the Invention"). O'Rourke et al. teach that antibody ligands may be either polyclonal sera or monoclonal antibodies (see entire document, e.g., column 5, especially lines 40-50). TSE containing aliquots equivalent to 125 mg starting material were electrophoresed through a 15% polyacrylamide mini-gel and transferred to PVDF membranes. The filters were developed with monoclonal antibody or a control antibody, goat anti-mouse IgG-HRPO, and a chemiluminescent substrate (see column 10, lines 34-65).

Korth et al. detects TSE based upon a monoclonal antibody that is specific for the prion form of PrP (the causative agent in TSEs) versus the cellular form of PrP (see entire document, e.g. Abstract). Korth et al. teach that this antibody can be used to identify the prion form of PrP directly, thus providing a basis for a TSE test in living humans or animals, by lowering the

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detection threshold needed (see especially paragraph preceding "Methods" on page 77). Thus Kuroda et al. teach that both B cells and T cells can transmit TSE, and Manuelidis et al. teach that it is important to focus on these cellular populations to increase the sensitivity of assays for TSE infectivity.

Both O'Rourke et al. and Korth et al. teach methods of detecting the disease form of prion protein after proteinase K digestion followed by SDS-Page electrophoresis and blotting onto a membrane. One of ordinary skill in the art would have had a high expectation of success in applying the techniques taught by O'Rourke et al. or Korth et al. to the infected tissue disclosed by Kuroda et al. or Manuelidis et al. It would have been obvious at the time the invention was made to improve the sensitivity of the TSE tests by collecting samples containing B cells and/or T cells and testing for the presence of TSE using an antibody-based system. The ordinary artisan at the time the invention was made would have been motivated to this in order to avoid having to utilize animals in order to test for infectivity in the B and/or T cell population. The ordinary artisan at the time the invention was made would have reasonably expected that concentrating a cell type known to be infected with the TSE agent would increase the sensitivity of detection assays, including antibody-based assays. In addition, it was well known in the art at the time the invention was made that once an antibody was developed, the antibody could be used with a reasonable expectation of success to detect an antigen on intact cells, as in a buffy coat of whole blood, by either mounting them on slides for immunohistochemical analysis; or by using other techniques well known in the art at the time the invention was made for intact cell analysis with antibodies. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

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### Claim Rejections - 35 USC § 112

The rejection of claims 35-37 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement **is withdrawn** in view of Applicants' amendments to the claims.

The rejection of claims 35-37 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn** in view of Applicants' amendments to the claims.

#### Conclusion

No claims allowed.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989). The Group 1600 Official Fax number is: (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <a href="http://pair-direct.uspto.gov">http://pair-direct.uspto.gov</a>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.

ULRIKE WINKLER, PH.D.

PRIMARY EXAMINER